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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/891,793 | 06/26/2001 | David J. Ecker | IBIS-0368 | 1490 |

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| EXAMINER | |
|---|---|
| FREDMAN, JEFFREY NORMAN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1637 | |

DATE MAILED: 03/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/891,793 | ECKER ET AL. | |
| | Examiner | Art Unit | |
| | Jeffrey Fredman | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on *24 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *69-100* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *69-100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/24/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 27, 2005 has been entered.

### Status

Applicant should note that the Art Unit and examiner have changed.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

### *Claim Interpretation*

2. As a preliminary issue, the claims must be interpreted before proceeding with the prior art analysis. The phrase "molecular mass" appears repeatedly in the claims and specification but no definition of this term was found. At page 9, the term is used in a manner which indicates that "any technique known in the art" can be used for the mass measurement. Therefore, the term is broadly read to encompass any mode of determination of molecular mass, including mass determinations by sizing on gel electrophoresis, as well as mass spectrometry, which is the clearly preferred mode of analysis.

The term "database" is also repeatedly used. The term is not defined in the specification. The ordinary meaning of "database" is a "collection of information". Any collection of information, such as a set of reference nucleic acid positions, would satisfy this claim limitation.

***Claim Rejections - 35 USC § 102***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 69-74, 79, 80, 82-90, 95, 96 and 98-100 are rejected under 35 U.S.C. 102(b) as being anticipated by Fluit et al (WO 95/13396).

Fluitt teaches a method of claims 69 and 85 of providing bacterial bioagent characterizing information (see abstract), comprising:

(a) *measuring or calculating a plurality of molecular masses corresponding to a plurality of amplification products* (see page 9, lines 1-15, where mobility is measured by gel electrophoresis which provides a measure of molecular mass)

*wherein the amplification products are 46 to 166 nucleobases in length* (see page 17, lines 1-2 and line 20, where the amplification product of the E5/ER6 primer set is 95 basepairs),

*and wherein the amplification products are obtained by amplification of a segment of bacterial nucleic acid with a primer pair that hybridizes to nucleic acid of about one hundred or more bacterial bioagents at conserved regions that flank an*

*intervening variable region* (see page 8, line 35 to page 9, line 16, where Fluitt teaches selection of universal primers to conserved 16S rRNA sequences which flank species specific (ie variable) regions. Also, a blast search (attached) of the ER5/ER6 primer set showed 1,227 bioagent hits with this primer pair (and BLAST limits the numbers of hits)),

(b) *interrogating a database with an identification query, wherein the identification query comprises a measured molecular mass of an amplification product 46 to 166 nucleobases in length of nucleic acid of a bacterial bioagent obtained upon amplification with the primer pair, and wherein the database comprises at least some members of the measured or calculated plurality of molecular masses of step a) wherein each member of the plurality of measured or calculated molecular masses is indexed to bacterial bioagent characterizing information* (see page 3, lines 29-31, where the electrophoresed positions of the amplified nucleic acids, amplified by the method of Fluitt, are compared with a set of reference nucleic acids (which is the database), also see page 7, lines 8-11 and page 11, lines 4-6, which discuss the use of an automatic DNA sequencer),

(c) *delivering a response that comprises the bacterial bioagent characterization information generated by comparison of the measured molecular mass of step b) with the measured or calclulated molecular masses of step a) contained in the database* (see page 3, lines 29-31, where the identity of the bacteria is determined by the comparison with a reference sample and page 24, lines 5-18, where the SS-DNA patterns were found to be species specific).

With regard to claims 70, 86, Fluitt teaches the use of 16S rRNA nucleic acid targets (see page 17, lines 25-27).

With regard to claims 71, 73, 79, 87, 89, 95, Fluitt teaches characterizing the bioagents down to the species level, which will have less than 5% sequence identity, which will include the genus name (see page 24, lines 5-6).

With regard to claims 72, 88, Fluitt teaches genus names including Acinetobacter (see page 23, line 19).

With regard to claims 74, 90, Fluitt teaches strain identification (see page 23, line 24, where a Salmonella strain, subsp. enterica is detected).

With regard to claims 80, 96, Fluitt teaches the use of FITC labeled primers, where the nucleobase with the FITC attached would be modified (see page 10, lines 12-22).

With regard to claims 82, 83, 98, 99, Fluitt teaches analysis of Shigella dysentarieae and Shigella flexneri (see page 23, lines 22-24).

With regard to claims 84, 100, Fluitt teaches primers ER5/ER6 which have more than 80% sequence identity over 1,277 bioagents as shown by the attached alignment.

### *Claim Rejections - 35 USC § 103*

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 75, 76, 91 and 92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fluit et al (WO 95/13396) in view of Iliff et al (U.S. Patent 6,475,143).

Fluitt teaches a method of claims 69 and 85 of providing bacterial bioagent characterizing information (see abstract), comprising:

(a) *measuring or calculating a plurality of molecular masses corresponding to a plurality of amplification products* (see page 9, lines 1-15, where mobility is measured by gel electrophoresis which provides a measure of molecular mass)

*wherein the amplification products are 46 to 166 nucleobases in length* (see page 17, lines 1-2 and line 20, where the amplification product of the E5/ER6 primer set is 95 basepairs),

*and wherein the amplification products are obtained by amplification of a segment of bacterial nucleic acid with a primer pair that hybridizes to nucleic acid of about one hundred or more bacterial bioagents at conserved regions that flank an intervening variable region* (see page 8, line 35 to page 9, line 16, where Fluitt teaches

selection of universal primers to conserved 16S rRNA sequences which flank species specific (ie variable) regions. Also, a blast search (attached) of the ER5/ER6 primer set showed 1,227 bioagent hits with this primer pair (and BLAST limits the numbers of hits)),

(b) *interrogating a database with an identification query, wherein the identification query comprises a measured molecular mass of an amplification product 46 to 166 nucleobases in length of nucleic acid of a bacterial bioagent obtained upon amplification with the primer pair, and wherein the database comprises at least some members of the measured or calculated plurality of molecular masses of step a) wherein each member of the plurality of measured or calculated molecular masses is indexed to bacterial bioagent characterizing information* (see page 3, lines 29-31, where the electrophoresed positions of the amplified nucleic acids, amplified by the method of Fluitt, are compared with a set of reference nucleic acids (which is the database), also see page 7, lines 8-11 and page 11, lines 4-6, which discuss the use of an automatic DNA sequencer),

(c) *delivering a response that comprises the bacterial bioagent characterization information generated by comparison of the measured molecular mass of step b) with the measured or calclulated molecular masses of step a) contained in the database* (see page 3, lines 29-31, where the identity of the bacteria is determined by the comparison with a reference sample and page 24, lines 5-18, where the SS-DNA patterns were found to be species specific).

Fluitt does not teach providing the information over a network such as the internet.

Iliff teaches internet based computer diagnosis (see column 30, lines 1-14) as well as classical diagnosis by a physician (see column 6, lines 16-27) using tests such as PCR (see column 7, lines 27-29).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to transmit the bioagent characterization information determined by the method of Fluitt over the internet or other networks to patients or physicians as taught by Iliff, since Iliff notes that "If the public had universal, unrestricted, and easy access to medical information, many diseases could be prevented. Likewise, the early detection and treatment of numerous diseases could keep many patients from reaching the advanced stages of illness, the treatment of which is a significant part of the financial burden attributed to our nation's health care system. (see column 1, lines 45-52)." So an ordinary practitioner would be motivated to provide infectious disease information over networks in order to permit early detection and treatment of the bacterial disease.

Separately, in the classic diagnostic situation, an ordinary practitioner would have been motivated to transmit diagnostic information to a physician over the internet or a local area network since such networks are known for use in transmitting diagnostic data as taught by Iliff and the ordinary practitioner would recognize that the use of the internet would permit increase efficiency and accuracy in the transmission of information

such as the specific bioagent identification taught by Fluitt from a medical laboratory to a physicians office or hospital.

7. Claims 77, 78, 93 and 94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fluit et al (WO 95/13396) in view of Muddiman et al (Anal. Chem. (1996) 68:3705-3712).

Fluitt teaches the limitations of claims 69-74, 79, 80, 82-90, 95, 96 and 98-100 as discussed above.

Fluitt does not teach the use of mass spectrometry in the detection.

Muddiman teaches a method of identifying a bioagent in a sample (see abstract), comprising:

(a) determining a first molecular mass of a first amplification product of a first bioagent identifying amplicon from the sample (see page 3707, column 1, where the are drawn to the 16S and 23S rRNA sequences, which are variable at some level at those locations and page 3707, column 2)

(b) comparing the first molecular mass to a second molecular mass of a second bioagent identifying amplicon (see page 2694, column 2, where identical primers were used to amplify multiple amplicons) wherein both first and second amplicons are correlative (see figures 2,-5 where the masses of two different species are compared).

Muddiman uses FT-ICR mass spectrometry with ESI (see page 3707, column 2).

Muddiman teaches that the bioagent is a Bacilli bacterium (see abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the Mass spectrometry method of Muddiman in the analytical method of Fluitt since Muddiman teaches "The molecular weights of the PCR products determined by nucleotide sequence and MS analysis were in excellent agreement, and several PCR products were analyzed where mass differences corresponding to single base substitutions could be accurately assigned. These assignments were possible due to the high mass precision, accuracy, and resolution FTICR inherently affords. This constitutes the flrst report demonstrating the ionization and detectlon of PCR products by mass spectrometry with mass precision and accuracy for assigment of such modifications or substitutions. (see abstract)."

Muddiman further notes "These results serve to demonstrate the speed, mass accuracy, and precision of the PCR product isolation schemes used and the general applicability of this approach (see page 3712, column 1)."

So an ordinary practitioner would have been motivated to detect the PCR products of Fluitt with the FTICR approach of Muddiman in order to improve the speed, mass accuracy and precision of the analysis and in particular due to the excellent agreement of sequencing and MS analysis.

8. Claims 81 and 97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fluit et al (WO 95/13396) in view of Lebedev et al (Genetic Analysis: Biomolecular Engineering (1996) 13:15-21).

Fluitt teaches the limitations of claims 69-74, 79, 80, 82-90, 95, 96 and 98-100 as discussed above.

Fluitt does not teach the use of the specific analogs of claims 81 and 97

Lebedev teaches the use of oligonucleotides with 2-aminoadenine (which STN Registry number RN 1904-98-9 indicates is an alternate name for 2, 6 diaminopurine) in PCR amplification (see abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute some 2,6 diaminopurine (2-aminoadenine) into the PCR reaction of Fluitt since Lebedev teaches that the nucleotide is useful "when primer binding is blocked by DNA secondary structure involving a primer binding site (see abstract)" and that the nucleotide has "highedr than normal affinity for complementary sequences (see abstract)". Since Fluitt is interested in amplifying the 16S rRNA which has significant secondary structure, the use of the 2-aminoadenine nucleotide will enhance the amplification of these sequences since it is useful when secondary structure is a problem. The ordinary practitioner would have been motivated by Lebedev to use 2, 6 diaminopurine in order to improve affinity of the PCR primers, particularly when amplifying a sequence such as Fluitt's which has significant secondary structure.

***Double Patenting***

9. Claims 69-100 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims

59,60,62,63,66,69-76 and 79-94 of copending Application No. 10/156,608. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application claims are virtually identical to the current claims, differing only in that the current claims are broader. The current claims are there a genus which encompasses the species claimed in copending Application 10/156,608 where the species anticipates the generic claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 69-100 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of copending Application No. 10/660,997 in view of Muddiman. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application claims represent a species of the current claims in which specific biowarfare organisms are selected. Muddiman teaches selection of Bacillus including bacillus anthracis. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the method of claims 1-28 of copending Application No. 10/660,997 with Muddiman in order to detect organisms of interest such as Anthrax.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Given the large number of related cases which show up on PALM, many of which are abandoned, Applicant is requested to comply with 37 CFR 1.56 by identification of copending applications, particularly applications close to issuance, which raise double patenting issues.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637
3/2/06